C:\STNEXP4\QUERIES\09763216.str

```
chain nodes :
   16 18 19 20 21
ring nodes :
   1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
chain bonds :
   12-18 15-16 18-19 18-20 20-21
ring bonds :
   1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 11-12 11-15
   12-13 13-14 14-15
exact/norm bonds :
   1-2 1-6 2-3 3-4 4-5 11-12 11-15 12-13 12-18 13-14 14-15 18-19
   18-20 20-21
exact bonds :
   15-16
normalized bonds :
   5-6 5-7 6-10 7-8 8-9 9-10
Match level :
   1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom
```

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS

```
Welcome to STN International! Enter x:x
```

```
LOGINID:
ssspta1611hxl
LOGINID:
PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2
```

```
NEWS 1
                  Web Page URLs for STN Seminar Schedule - N. America
         Apr 08
NEWS 2
                  "Ask CAS" for self-help around the clock
NEWS 3
         Apr 09
                  BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 4
NEWS 5
         Apr 09
                  ZDB will be removed from STN
         Apr 19
                 US Patent Applications available in IFICDB, IFIPAT, and
IFIUDB
NEWS 6 Apr 22 Records from IP.com available in CAPLUS, HCAPLUS, and
ZCAPLUS
NEWS 7
         Apr 22
                 BIOSIS Gene Names now available in TOXCENTER
NEWS 8
         Apr 22
                 Federal Research in Progress (FEDRIP) now available
NEWS
         Jun 03
                 New e-mail delivery for search results now available
NEWS 10
         Jun 10
                 MEDLINE Reload
NEWS 11
         Jun 10
                 PCTFULL has been reloaded
         Jul 02
NEWS 12
                  FOREGE no longer contains STANDARDS file segment
NEWS 13
         Jul 22
                 USAN to be reloaded July 28, 2002;
                  saved answer sets no longer valid
NEWS 14
         Jul 29
                  Enhanced polymer searching in REGISTRY
NEWS 15
         Jul 30
                 NETFIRST to be removed from STN
NEWS 16
         Aug 08
                 CANCERLIT reload
NEWS 17
         Aug 08
                 PHARMAMarketLetter (PHARMAML) - new on STN
NEWS 18
         Aug 08
                 NTIS has been reloaded and enhanced
NEWS 19
         Aug 19
                 Aquatic Toxicity Information Retrieval (AQUIRE)
                  now available on STN
NEWS 20
         Aug 19
                 IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21
         Aug 19
                 The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22
         Aug 26
                 Sequence searching in REGISTRY enhanced
NEWS 23
         Sep 03
                 JAPIO has been reloaded and enhanced
NEWS 24
         Sep 16
                 Experimental properties added to the REGISTRY file
NEWS 25
         Sep 16
                 Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 26
         Sep 16
                 CA Section Thesaurus available in CAPLUS and CA
NEWS 27
         Oct 01
                 CASREACT Enriched with Reactions from 1907 to 1985
NEWS 28
                 EVENTLINE has been reloaded
         Oct 21
NEWS EXPRESS October 14 CURRENT WINDOWS VERSION IS V6.01,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
NEWS HOURS
               STN Operating Hours Plus Help Desk Availability
NEWS INTER
              General Internet Information
NEWS LOGIN
               Welcome Banner and News Items
NEWS PHONE
               Direct Dial and Telecommunication Network Access to STN
```

NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 13:53:50 ON 22 OCT 2002

=> fil reg
COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 0.21 0.21

FULL ESTIMATED COST

FILE 'REGISTRY' ENTERED AT 13:54:01 ON 22 OCT 2002 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2002 American Chemical Society (ACS)

Property values tagged with IC are from the ${\tt ZIC/VINITI}$ data file provided by InfoChem.

STRUCTURE FILE UPDATES: 21 OCT 2002 HIGHEST RN 463926-32-1 DICTIONARY FILE UPDATES: 21 OCT 2002 HIGHEST RN 463926-32-1

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>Testing the current file.... screen

ENTER SCREEN EXPRESSION OR (END):end

=> Uploading C:\STNEXP4\QUERIES\09763216.str Print selected from Online session

Page 3

L1 STRUCTURE UPLOADED

=> que L1

L2 QUE L1

=> d 11

L1 HAS NO ANSWERS

L1 STR

Structure attributes must be viewed using STN Express query preparation.

=> s 11

SAMPLE SEARCH INITIATED 13:54:22 FILE 'REGISTRY' SAMPLE SCREEN SEARCH COMPLETED - 568 TO ITERATE

100.0% PROCESSED 568 ITERATIONS

27 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 9931 TO 12789

PROJECTED ANSWERS: 229 TO 851

L3 27 SEA SSS SAM L1

=> d scan

L3 27 ANSWERS REGISTRY COPYRIGHT 2002 ACS

IN 2-Furancarboxamide, N-[2-hydroxy-1-(hydroxymethyl)-2-phenylethyl]-5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]- (9CI)

MF C30 H37 N O4

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=>Testing the current file.... screen

ENTER SCREEN EXPRESSION OR (END):end

=>

Uploading C:\STNEXP4\QUERIES\09763216.str

STRUCTURE UPLOADED

=> que L4

L5 QUE L4

=> d 14

L4 HAS NO ANSWERS

L4STR

Structure attributes must be viewed using STN Express query preparation.

=> s 14

SAMPLE SEARCH INITIATED 13:55:33 FILE 'REGISTRY' SAMPLE SCREEN SEARCH COMPLETED - 689 TO ITERATE

100.0% PROCESSED 689 ITERATIONS 24 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**

PROJECTED ITERATIONS:

12206 TO 15354 187 TO 773 PROJECTED ANSWERS: 773

L6 24 SEA SSS SAM L4

=> d scan

REGISTRY COPYRIGHT 2002 ACS L6 24 ANSWERS

IN 2-Furancarboxamide,

5-[(5,6,7,8-tetrahydro-3-methoxy-5,5,8,8-tetramethyl-2-

naphthalenyl)methyl]-N-(2,4,6-trimethoxyphenyl)-(9CI)MF C30 H37 N O6

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=> s 14 ful

FULL SEARCH INITIATED 13:55:48 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 12993 TO ITERATE

100.0% PROCESSED 12993 ITERATIONS SEARCH TIME: 00.00.02

359 ANSWERS

L7 359 SEA SSS FUL L4

=> fil caplus COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 141.04 141.25

FULL ESTIMATED COST

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FILE COVERS 1907 - 22 Oct 2002 VOL 137 ISS 17 FILE LAST UPDATED: 21 Oct 2002 (20021021/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> s 17

L8

2 L7

=> d ibib abs 1-

YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y

ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS

2002:200606 CAPLUS

ACCESSION NUMBER: DOCUMENT NUMBER:

137:73535

TITLE:

Effect of testosterone suppression on the

pharmacokinetics of a potent GnRH receptor antagonist

AUTHOR(S):

Iatsimirskaia, Eugenia A.; Gregory, Margaret L.; Anderes, Kenna L.; Castillo, Rosemary; Milgram, K. Eric; Luthin, David R.; Pathak, Ved P.; Christie, Lance C.; Vazir, Haresh; Anderson, Mark B.; May, John

CORPORATE SOURCE:

Metabolism,

Department of Pharmacokinetics, Dynamics &

Pfizer Global Research and Development / Agouron Pharmaceuticals, Inc., San Diego, CA, 92121, USA Pharmaceutical Research (2002), 19(2), 202-208

SOURCE:

CODEN: PHREEB; ISSN: 0724-8741 Kluwer Academic/Plenum Publishers

PUBLISHER: DOCUMENT TYPE:

LANGUAGE:

Journal English

AΒ The expression of cytochrome P 450 enzymes (CYPs) in animals and humans is

under complex hormonal regulation. Chronic treatment with drugs that alter sex hormone levels such as gonadotropin-releasing hormone (GnRH) receptor agonists or antagonists may affect the expression of hormone-dependent CYPs, and as a result the pharmacokinetics of drugs metabolized by them. Enzyme kinetic parameters were obtained by incubating the GnRH antagonist AG-045572 (0.1-30 .mu.M) with human or rat liver microsomes or expressed CYP3A4 and CYP3A5. The pharmacokinetics of AG-045572 (10 mg/kg i.v. or 20 mg/kg orally) were studied in intact male, female, and castrated male rats and in male rats pretreated with AG-045572

for 4 days. AG-045572 is metabolized by CYP3A in both rats and humans. The Km values were similar in male and female human liver microsomes, female rat liver microsomes, and expressed CYP3A4 and CYP3A5 (0.39, 0.27, 0.28, 0.25, and 0.26 .mu.M, resp.). The Km in male rat liver microsomes was $1.5\,$.mu.M, suggesting that in male and female rats AG-045572 is metabolized by different CYP3A isoenzymes. The oral bioavailability of AG-045572 in intact male rats was 8%, while in female or castrated male rats it was 24%. Pretreatment of intact male rats with AG-045572 i.m.

for

4 days resulted in suppression of testosterone to castrate levels, accompanied by an increase in the oral bioavailability of AG-045572 to

27%. In the same expt., the male-specific pulsatile pattern of growth hormone remained unchanged, with slightly elevated basal levels. The potent GnRH receptor antagonist AG-045572 is metabolized by hormone-dependent CYP3A. As a result, suppression of testosterone by pretreatment with AG-045572 "feminized" its own pharmacokinetics. REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2000:241135 CAPLUS DOCUMENT NUMBER: 132:279106

TITLE:

Non-peptide GnRH agents, methods and intermediates

for

GI

their preparation

INVENTOR(S):

Anderson, Mark Brian; Vazir, Haresh N.; Luthin, David Robert; Paderes, Genevieve Deguzman; Pathak, Ved P.; Christie, Lance Christopher; Hong, Yufeng; Tompkins,

Eileen Valenzuela; Li, Haitao; Faust, James Agouron Pharmaceuticals, Inc., USA; et al.

PATENT ASSIGNEE(S):

PCT Int. Appl., 444 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

```
PATENT NO.
                          KIND DATE
                                                  APPLICATION NO. DATE
                          ----
      WO 2000020358 A2 20000413
WO 2000020358 A3 20001116
                                                    WO 1999-US18790 19990820
          W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
               DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,
               JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,
               MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
           RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
               ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
               CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
          9913374 A 20010515 BR 1999-13374 19990820
1105120 A2 20010613 EP 1999-968010 19990820
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO
      BR 9913374
      EP 1105120
      NO 2001000309
                         A
                                  20010411
                                                    NO 2001-309
                                                                         20010119
      LV 12732
                            В
                                  20020320
                                                    LV 2001-45
                                                                         20010316
      LT 4904
                           В
                                  20020425
                                                    LT 2001-24
                                                                         20010319
                                                 US 1998-97520P P 19980820
WO 1999-US18790 W 19990820
PRIORITY APPLN. INFO.:
OTHER SOURCE(S): MARPAT 132:279106
```

AB Non-peptide GnRH agents capable of inhibiting the effect of gonadotropin-releasing hormone are described. The compds. and their pharmaceutically acceptable salts, multimers, prodrugs, and active metabolites are suitable for treating mammalian reproductive disorders

and

steroid hormone-dependent tumors as well as for regulating fertility, where suppression of gonadotropin release is indicated. The compds. include those of formula I [X = C:O, C:S, S:O, or SO2; Het = 5-membered NOS-heterocycle; R1, R2 = H, alkyl; R3-R7 = H, halo, (un) substituted alkyl, aryl, heteroaryl, CH2OR, OR, CO2R; R = alkyl, aryl, etc.; adjacent rings positions such as R6R7 may form (un) substituted 5- or 6-membered ring with up to 4 heteroatoms; R8 = lipophilic moiety such as alkyl,

aryl,

CH2OR, OR, etc.; R9 = H, (un)substituted alkyl]. Methods and intermediates for synthesizing the compds. are also described. For instance, 4,4,7-trimethylchroman (prepn. given) was alkylated in the 6-and 8-positions using Et 5-(chloromethyl)-2-furoate (46% total yield),

and

the resulting esters were hydrolyzed to a mixt. of acids. This unsepd. ${\tt mixt.}$ was treated with SOC12 and amidated with

2,4,6-trimethoxyphenylamine-

HCl to give the invention compd. II and its chroman-6-position isomer, which were sepd. by HPLC. Several compds. exhibited high affinity (<100 nM) at human GnRH receptors. The compds. antagonized GnRH-stimulated inositol phosphate accumulation in cells with recombinant human GnRH receptors, and an example compd. reduced plasma LH levels in castrated male rats. Various biol. data for several hundred compds. are given.

=> d his

(FILE 'HOME' ENTERED AT 13:53:50 ON 22 OCT 2002)

FILE 'REGISTRY' ENTERED AT 13:54:01 ON 22 OCT 2002	
L1 STRUCTURE UPLOADED	
L2 QUE L1 L3 27 S L1	
L4 STRUCTURE UPLOADED	
L5 QUE L4	
L6 24 S L4 L7 359 S L4 FUL	
L/ 339 S L4 FUL	
FILE 'CAPLUS' ENTERED AT 13:55:55 ON 22 OCT 2002	
L8 2 S L7	
=> logoff	
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF	
LOGOFF? (Y)/N/HOLD:y	

COST IN U.S. DOLLARS

SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST

SINCE FILE TOTAL
ENTRY SESSION
6 16

FULL ESTIMATED COST 6.16 147.41

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION CA SUBSCRIBER PRICE -1.24 -1.24

STN INTERNATIONAL LOGOFF AT 13:58:31 ON 22 OCT 2002